MELANOCORTIN MC3 AND MC4 RECEPTOR EXPRESSION AND MELANOCORTIN EFFECTS IN FETAL AND EARLY POSTNATAL RAT BRAIN, W. Lichtensteiger, V. Kistler-Heer, M.E. Lauber and M. Schlumpf, Institute of Pharmacology, University of Zürich, CH-8057 Zürich, Switzerland.

Melanocortins are supposed to be involved in ontogeny and regeneration of nervous tissue. We recently reported on region- and stage-specific developmental patterns of binding sites for [^{125}I]Nle, D-Phe-α-MSH (^{125}I-NDP) in rat central nervous system, cranial nerve ganglia and sympathetic ganglia, with a number of regions exhibiting marked transient peaks of receptor expression (Lichtensteiger et al., Dev. Brain Res. 91:93, 1996). NDP binds to the main melanocortin receptors found in brain, i.e., the MC3 and MC4 receptor, with comparable affinity. In subsequent in situ hybridization experiments using ^{33}P-labeled oligonucleotides, we so far have detected MC3 mRNA only in postnatal rat brain. Ventromedial and arcuate hypothalamic nuclei, which exhibit a slow postnatal development of ^{125}I-NDP binding sites, contain MC3 mRNA during the first postnatal week. In contrast, MC4 mRNA is found in the majority of regions with high fetal and perinatal levels of ^{125}I-NDP binding. This suggests that the MC4 receptor may represent an important type of melanocortin receptor during prenatal ontogeny. Possible developmental actions of melanocortins were studied in cell cultures of striatum, a region exhibiting a high perinatal peak of ^{125}I-NDP binding with a subsequent drop to low levels in caudate-putamen and persistent elevated levels in accumbens and olfactory tubercle. Serum-free cultures of dissociated cells of striatum, combined with midbrain, were prepared from fetuses of time-pregnant rats during the rising phase of striatal MC4 receptor expression (gestational day 18). Preliminary data indicate a small to moderate increase of neurofilament content of the cultures (determined by ELISA) following short-term exposure to α-MSH and NDP, while the effect of ACTH is uncertain over an extended concentration range. GAP43 content remained unaffected. Additional developmental markers are being investigated. The results are suggestive of a developmental action of melanocortins at brain level, but require further analysis.